TRANSLATION

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Form PCT/IPEA/416
V 7588/RN		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/010695	23.09.2004	23.09.2003
International Patent Classification (IPC) or national classification and IPC		
C12Q1/70		
Applicant		
VERMICON AG		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 21 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *(sent to the applicant and to the International Bureau)* a total of _____ sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____ , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
Name and mailing address of the IPEA/EP Facsimile No.	Authorized officer Telephone No.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (Rule 12.3 and 23.1(b))

☐ publication of the international application (Rule 12.4)

☐ international preliminary examination (Rule 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-77 as originally filed/furnished

pages* _____ received by this Authority on _____

pages* _____ received by this Authority on _____

☒ the claims:

nos. 1-56 as originally filed/furnished

nos.* _____ as amended (together with any statement) under Article 19

nos.* _____ received by this Authority on _____

nos.* _____ received by this Authority on _____

☒ the drawings:

sheets _____ as originally filed/furnished

sheets* _____ received by this Authority on _____

sheets* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____

☐ the claims, nos. _____

☐ the drawings, sheets/figs _____

☐ the sequence listing *(specify)*: _____

☐ any table(s) related to sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 3-40, 43-53 (all in full), 1, 54-56 (all in part)

because:

☐ the said international application, or the said claims Nos. _____
relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 3-40, 43-53 (all in full), 1, 54-56 (all in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
☐ has not been furnished
☐ does not comply with the standard

the computer readable form
☐ has not been furnished
☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees the applicant has:

   ☐ restricted the claims.

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ neither restricted the claims nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is:

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1, 54-56 (all in part), 2, 41, 42 (all in full)

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1, 54-56 (all in part), 2, 41, 42 (all in full)	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1, 54-56 (all in part), 2, 41, 42 (all in full)	NO
Industrial applicability (IA)	Claims	1, 54-56 (all in part), 2, 41, 42 (all in full)	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1: WO 02/103043 A (VERMICON AG; BEIMFOHR, CLAUDIA; SNAIDR, JIRI) 27 December 2002 (2002-12-27)

D2: WO 00/77259 A (BOSTON PROBES, INC) 21 December 2000 (2000-12-21)

D3: WO 01/53316 A (E. & J. GALLO WINERY) 26 July 2001 (2001-07-26)

D4: JAMES S A ET AL: "Use of an rRNA internal transcribed spacer region to distinguish phylogenetically closely related species of the genera Zygosaccharomyces and Torulaspora" INTERNATIONAL JOURNAL OF SYSTEMATIC BACTERIOLOGY, SOCIETY FOR GENERAL MICROBIOLOGY, READING, GB, Vol. 46, No. 1, January 1996 (1996-01), pages 189-194, XP002102425 ISSN: 0020-7713

D5: DATABASE EMBL [Online] 2 November 2002 (2002-11-02), "KD2317.p1 Kluyveromyces delphensis Random Genomic Library Kluyveromyces delphensis genomic clone KD2317, DNA sequence." XP002319768 Retrieved

from EBI accession no. EM_PRO:BZ303298 Database accession no. BZ303298

D6: DATABASE EMBL [Online] 2 November 2002 (2002-11-02), "CG0215.f1 Candida glabrata Random Genomic Library Candida glabrata genomic clone CG0215, DNA sequence." XP002319769 Retrieved from EBI accession no. EM_PRO:BZ293221 Database accession no. BZ293221

D7: WO 98/55649 A (CHIRON DIAGNOSTICS CORPORATION; SANDHU, GURPREET, S; KLINE, BRUCE, C) 10 December 1998 (1998-12-10)

D8: MORRISON L E ET AL: "Solution-phase detection of polynucleotides using interacting fluorescent labels and competitive hybridization" ANALYTICAL BIOCHEMISTRY, ACADEMIC PRESS, NEW YORK, NY, US, Vol. 183, No. 2, December 1989 (1989-12), pages 231-244, XP002113097 ISSN: 0003-2697

2.1 **INVENTIVE STEP** (PCT Article 33(3))

2.2 Regarding independent claim 1, document D2 is considered the prior art closest to the subject matter of claim 1. D2 discloses a method for detecting beverage-spoiling micro-organisms of the *Zygosaccharomyces* genus in a sample, detection being carried out using an oligonucleotide probe (see page 5, paragraph 3 and example 12).

2.3 The subject matter of claim 1 thus differs from that of the closest prior art in that the probe

has a different nucleic acid sequence.

2.4 This difference does not appear to be associated with any unexpected technical effect.

2.5 The present invention can therefore be considered to address the problem of developing an alternative probe for detecting *Zygosaccharomyces*.

2.6 The solution proposed in claim 1 of the present application cannot be considered inventive (PCT Article 33(3)) for the following reasons:

2.6.1 Numerous probes for detecting *Zygosaccharomyces* are known (see D2, example 12 and D3, SEQ ID Nos. 20, 21, 25, 26 and example 5). It is also generally known that the 18S rRNA gene is suitable for detecting *Zygosaccharomyces* (see D4, the entire document).

2.6.2 Since the claimed probe does not have an unexpected technical effect, the choice of probe, in view of the fact that the target sequence is well-known in the art (see D4), is considered a non-inventive selection from alternative possibilities.

2.6.3 Consequently, the subject matter of claim 1 does not involve an inventive step (PCT Article 33(3)).

2.7 The same reasoning applies to independent claim 56; since the probe with SEQ ID No. 1 is not

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

inventive, the kit containing that probe is also not inventive (PCT Article 33(3)).

2.8 Dependent claims 2, 41, 42, 54 and 55 do not contain any features which, in combination with the features of any claim to which they refer, meet the PCT requirements for inventive step; see documents D1, D2, D7 and D8 and the relevant passages of text indicated in the search report.

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Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

Application No. Patent No.	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO03/097868	27.11.2003	15.03.2003	15.05.2002
WO2004/063699	29.07.2004	02.12.2003	02.12.2002

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

The sequence listing in the description, pages 1-203 as originally filed/furnished

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**
Continuation of:

1 Box IV
Lack of unity of invention

1.1 This Authority has determined that the international application contains multiple inventions or groups of invention which are not linked by a single general inventive concept (PCT Rule 13.1), as follows:

Invention 1:
Claims 1, 54-56 (in part), 2, 41, 42 (in full):

Methods and kits for detecting *Zygosaccharomyces*, detection being carried out using at least one oligonucleotide probe having SEQ ID 1.

Invention 2:
Claims 1, 54-56 (in part), 3 (in full)

Methods and kits for detecting *Zygosaccharomyces bailii*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 5 to 21.

Invention 3:
Claims 1, 54-56 (in part), 4 (in full)

Methods and kits for detecting *Zygosaccharomyces fermentati*, detection being carried out using at

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least one oligonucleotide probe having SEQ ID 22.

Invention 4:
Claims 1, 54-56 (in part), 5 (in full)

Methods and kits for detecting *Zygosaccharomyces microellipsoides*, detection being carried out using at least one oligonucleotide probe having SEQ ID 23 or 24.

Invention 5:
Claims 1, 54-56 (in part), 6 (in full)

Methods and kits for detecting *Zygosaccharomyces mellis*, detection being carried out using at least one oligonucleotide probe having SEQ ID 25 to 75.

Invention 6:
Claims 1, 54-56 (in part), 7, 8 (in full)

Methods and kits for detecting *Zygosaccharomyces rouxii*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 76 to 126.

Invention 7:
Claims 1, 54-56 (in part), 9 (in full)

Methods and kits for detecting *Zygosaccharomyces bisporus*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 128 to 142.

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Invention 8:
Claims 1, 54-56 (in part), 10 (in full)

Methods and kits for detecting *Hanseniaspora uvarum*, detection being carried out using at least one oligonucleotide probe having SEQ ID 143 or 144.

Invention 9:
Claims 1, 54-56 (in part), 11, 43, 44 (in full)

Methods and kits for detecting *Candida intermedia*, detection being carried out using at least one oligonucleotide probe having SEQ ID 145 or 146.

Invention 10:
Claims 1, 54-56 (in part), 12 (in full)

Methods and kits for detecting *Candida parapsilosis*, detection being carried out using at least one oligonucleotide probe having SEQ ID 148.

Invention 11:
Claims 1, 54-56 (in part), 13 (in full)

Methods and kits for detecting *Candida crusei*, detection being carried out using at least one oligonucleotide probe having SEQ ID 149.

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Invention 12:
Claims 1, 54-56 (in part), 14, 15 (in full)

Methods and kits for detecting *Brettanomyces bruxellensis*, detection being carried out using at least one oligonucleotide probe having SEQ ID 150 or 151.

Invention 13:
Claims 1, 54-56 (in part), 16 (in full)

Methods and kits for detecting *Brettanomyces naardenensis*, detection being carried out using at least one oligonucleotide probe having SEQ ID 152.

Invention 14:
Claims 1, 54-56 (in part), 17 (in full)

Methods and kits for the simultaneous detection of *membranaefaciens*, detection being carried out using at least one oligonucleotide probe having SEQ ID 153.

Invention 15:
Claims 1, 54-56 (in part), 18, 45, 46 (in full)

Methods and kits for the simultaneous detection of *Pichia minuta* and *Pichia anomala*, detection being carried out using at least one oligonucleotide probe having SEQ ID 154.

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Invention 16:
Claims 1, 54-56 (in part), 19 (in full)

Methods and kits for detecting *Saccharomyces exiguus*, detection being carried out using at least one oligonucleotide probe having SEQ ID 157.

Invention 17:
Claims 1, 54-56 (in part), 20 (in full)

Methods and kits for detecting *Saccharomyces ludwigii*, detection being carried out using at least one oligonucleotide probe having SEQ ID 158 or 159.

Invention 18:
Claims 1, 54-56 (in part), 21, 47, 48 (in full)

Methods and kits for detecting *Saccharomyces cerevisiae*, detection being carried out using at least one oligonucleotide probe having SEQ ID 160.

Invention 19:
Claims 1, 54-56 (in part), 22 (in full)

Methods and kits for detecting *Mucor racemosus*, detection being carried out using at least one oligonucleotide probe having SEQ ID 163.

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Invention 20:
Claims 1, 54-56 (in part), 23 (in full)

Methods and kits for detecting *Byssochlamys nivea*, detection being carried out using at least one oligonucleotide probe having SEQ ID 164.

Invention 21:
Claims 1, 54-56 (in part), 24 (in full)

Methods and kits for detecting *Neosartorya fischeri*, detection being carried out using at least one oligonucleotide probe having SEQ ID 165.

Invention 22:

Claims 1, 54-56 (in part), 25 (in full)

Methods and kits for the simultaneous detection of *Aspergillus fumigatus* and *A. fischeri*, detection being carried out using at least one oligonucleotide probe having SEQ ID 166.

Invention 23:
Claims 1, 54-56 (in part), 26 (in full)

Methods and kits for detecting *Talaromyces flavus*, detection being carried out using at least one oligonucleotide probe having SEQ ID 167.

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Invention 24:
Claims 1, 54-56 (in part), 27 (in full)

Methods and kits for the simultaneous detection of *Talaromyces bacillisporus* and *T. flavus*, detection being carried out using at least one oligonucleotide probe having SEQ ID 168.

Invention 25:
Claims 1, 54-56 (in part), 28 (in full)

Methods and kits for detecting *Lactobacillus collinoides*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 169 to 269.

Invention 26:
Claims 1, 54-56 (in part), 29 (in full)

Methods and kits for detecting *Leuconostoc*, detection being carried out using at least one oligonucleotide probe having SEQ ID 270 or 271.

Invention 27:
Claims 1, 54-56 (in part), 30 (in full)

Methods and kits for the simultaneous detection of *Leuconostoc mesenteroides* and *L. pseudomesenteroides*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 272 to 301.

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Invention 28:
Claims 1, 54-56 (in part), 31 (in full)

Methods and kits for detecting *Leuconostoc pseudomesenteroides*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 302 to 341.

Invention 29:
Claims 1, 54-56 (in part), 32 (in full)

Methods and kits for detecting *Oenococcus oeni*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 342 to 444.

Invention 30:
Claims 1, 54-56 (in part), 33 (in full)

Methods and kits for detecting *Weissella*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 445 to 495.

Invention 31:
Claims 1, 54-56 (in part), 34 (in full)

Methods and kits for detecting *Lactococcus*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 496 to 546.

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Invention 32:
Claims 1, 54-56 (in part), 35 (in full)

Methods and kits for the simultaneous detection of *Acetobacter* and *Gluconobacter*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 547 to 608.

Invention 33:
Claims 1, 54-56 (in part), 36 (in full)

Methods and kits for the simultaneous detection of *Acetobacter*, *Gluconobacter* and *Gluconoacetobacter*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 609 bis 842.

Invention 34:
Claims 1, 54-56 (in part), 37 (in full)

Methods and kits for detecting *Bacillus coagulans*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 843 to 932.

Invention 35:
Claims 1, 54-56 (in part), 38, 49, 50 (in full)

Methods and kits for detecting *Alicyclobacillus*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 933 to 1033.

Invention 36:
Claims 1, 54-56 (in part),39, 51, 52, 53(in full)

Methods and kits for detecting *Alicyclobacillus acidoterrestris*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 1037 to 1138.

Invention 37:
Claims 1, 54-56 (in part), 40 (in full)

Methods and kits for the simultaneous detection of *Alicyclobacillus cycloheptanicus* and *A. herbarius*, detection being carried out using at least one oligonucleotide probe having SEQ ID n, wherein n = 1142 to 1144.

1.2 In view of the fact that sequence-specific probes for detecting beverage-spoiling micro-organisms are already known from D1 (see claims 2, 4 and 8) and D2 (see claims 46 to 48), the problem addressed by the current application is that of developing further alternative sequence-specific probes for detecting beverage-spoiling micro-organisms. Since probes for detecting beverage-spoiling micro-organisms, for example *Zygosaccharomyces*, are already known in the art, based on the essential differences in the primary structures of the probes described in the application and in view of the lack of technical features which taking into consideration the prior

Supplemental Box

art can be regarded as special technical features, the International Examining Authority is of the opinion that the solutions (37 groups of probes that are specific to a micro-organism or a group of micro-organisms) do not involve any common inventive concept (PCT Rule 13.1). The requirement for unity of invention is therefore not satisfied.